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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,296	08/27/2001	Sithian Pandian	MBM1270	7256

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EXAMINER
WHISENANT, ETHAN C

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,296	PANDIAN ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 JAN 03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *5-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I (**Claims 1-4 and 25-29**) with traverse is acknowledged. Claims 5-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is noted that the applicant has traversed the restriction requirement, however, because the applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement has been reconsidered, is deemed proper and is therefore, herein made **FINAL**.

35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** The invention was described in –
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

3. **Claim(s) 1-4** are rejected under 35 U.S.C. 102(b) as anticipated by Urdea et al. [US Patent No. 5,124,246 (JUN 1992)].

Claim 1 is drawn to an amplification probe comprising at least two regions of nucleic acid sequence including at first sequence complementary to a sequence on a selected primary probe and a second region which is to include a plurality of discretely labalable sequence units. Note, that the examiner has interpreted the phrase "discretely labalable sequence units" to mean : a sequence unit that is capable of, under appropriate conditions, becoming labeled via hybridization to a labeled detection probe. This interpretation is based on a reading of the specification pp. 17-19 wherein the applicants have

explained what they intend by the phrase "amplification probe". It should also be noted that the limitations in claim 1 that are directed to the structure of the primary probe do not further limit the structure of the amplification probe, the product being claimed in Claim 1.

Urdea et al. teach linear or branched oligonucleotide multimers (i.e. oligo D in Figure 4) which are useful as amplifiers in biochemical assays. The multimers taught by Urdea et al. meet all of the limitations of the claimed amplification probe claimed in Claim 1. Urdea et al. describe their multimers beginning in Column 8. The multimers taught by Urdea et al. comprise at least two regions of nucleic acid sequence including at first sequence complementary to a sequence on a selected primary probe (i.e. oligo B in Figure 4) and a second region which is to include a plurality of discretely labalable sequence units (i.e. the "arms" of the multimer D). These "arms" are complementary to and hybridize with labeled detection probes (i.e. oligo E in Figure 4).

Claim 2 is drawn to an embodiment of Claim 1 wherein the number of discretely labalable sequence units ranges from 2 to 50.

Urdea et al. teach this limitation wherein they teach that the total number of oligonucleotide in a multimer will usually be in the range of 3 to 50 more usually 10 to 20. In addition, Urdea et al. teach that each oligonucleotide unit will normally be 15 to 50, preferably 15 to 30 nucleotides in length and have a GC content in the range of 40% to 60%.

Claim 3 is drawn to an embodiment of Claim 1 wherein each of the discretely labalable sequence units comprises a nucleotide sequence hybridizable to a complementary sequence on a labeled labeling probe.

Urdea et al. teach this limitation wherein they teach the hybridization of oligo E, a labeled labeling probe, to an "arm" of the multimer. See Figure 4 step 4-5.

Claim 4 is drawn to an embodiment of Claim 3 wherein the length of each discretely labalable sequence unit ranges from 16 to 100 nucleotides.

Urdea et al. teach this limitation wherein they teach that each oligonucleotide unit will normally be 15 to 50, preferably 15 to 30 nucleotides in length and have a GC content in the range of 40% to 60%.

4. **Claim(s) 1-4** are rejected under 35 U.S.C. 102(e) as anticipated by Segev et al. [US Patent No. 5,437,977 (AUG 1995)].

Claim 1 is drawn to an amplification probe comprising at least two regions of nucleic acid sequence including at first sequence complementary to a sequence on a selected primary probe and a second region which is to include a plurality of discretely labalable sequence units.

Segev et al. teach branched oligonucleotides (i.e. # 70 in Figure 4) which are useful as amplifiers in biochemical assays. The branched oligonucleotides taught by Segev et al. meet all of the limitations of the claimed amplification probe claimed in Claim 1. Segev et al. describe their branched oligonucleotides as bridging and/or developer molecules/probes, beginning in Column 6. The branched oligonucleotides taught by Segev et al. comprise at least two regions of nucleic acid sequence including a first sequence region complementary to a sequence on a selected primary probe and a second region which is to include a plurality of discretely labalable sequence units. In Segev et al. the second sequence region, which according to the claim, must include a plurality of discretely labalable sequence units, is the two branches of the bridging molecule or the developer molecule.

Claim 2 is drawn to an embodiment of Claim 1 wherein the number of discretely labelable sequence units ranges from 2 to 50.

Segev et al. teach this limitation wherein they teach that the number of branches on a linear developer probe is two while branched developer molecules will have more than two.

Claim 3 is drawn to an embodiment of Claim 1 wherein each of the discretely labalable sequence units comprises a nucleotide sequence hybridizable to a complementary sequence on a labeled labeling probe.

Segev et al. teach this limitation wherein they teach that the developer probes also act as label probes. See Column 6 and Figure 4.

Claim 4 is drawn to an embodiment of Claim 3 wherein the length of each discretely labalable sequence unit ranges from 16 to 100 nucleotides.

Segev et al. do not explicitly teach a sequence range for each discretely labalable sequence unit . However, Segev et al. do teach that the complementary sequence of each bridging/developer probe should comprise at least 6 contiguous nucleotide bases. In addition, Segev et al. teach in Columns 9-10 the preferred structure for their probes. Based on all of these teachings, therefore, it is inherent to the teaching of Segev et al. that the length of each discretely labalable sequence unit can fall within the

range of from 16 to 100 nucleotides. It would have been prima facie obvious to the skilled artisan upon a reading of Segev et al. that the length of each branch depended upon convenience, and the assay to be performed . Note, that Segev et al. teach that the primary probe and more importantly, the bridging molecule, is to preferably comprise 12-100 nucleotide bases.

35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

7. **Claim(s) 25-26** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al. [US Patent No. 5,124,246 (JUN 1992)], as applied to Claims 1-4 above, and further in view of Fliss et al. (AUG 1993).

Claim 25 is drawn to a reagent system for detecting a polynucleotide in a test sample which is to comprise four components:

[1]a primary nucleic acid probe that is to comprise at least one single stranded base sequence that is substantially complementary to the target sequence to be detected.

[2]an antibody reagent capable of binding to hybrids formed between the primary probe and any particular polynucleotide target sequence present in the sample. Said antibody reagent must be incapable of binding substantially to single stranded nucleic acids.
[3]an amplification probe comprising at least two regions of nucleic acid sequence including at first sequence complementary to a sequence on said primary probe and a second region which is to include a plurality of discretely labalable sequence units.
[4]a labeling probe which is to comprise a detectable label and sequence complementary to sequences on the amplification probe.

Urdea et al. teach a reagent system which comprises 3 of the 4 components of the claimed reagent system. The 3 components present in the reagent system taught by Urdea et al. include components 1, 3 and 4 of the claimed reagent system. Urdea et al. does not teach component 2, i.e. an antibody reagent capable of binding to hybrids formed between the primary probe and any particular polynucleotide target sequence present in the sample. However, Fliss et al. do teach an antibody reagent capable of binding to hybrids formed between a primary probe and its target sequence present in a biological sample. Note, that the antibody reagent taught by Fliss et al. is incapable of binding substantially to single stranded nucleic acids. See Fliss et al. Therefore, in the absence of an unexpected result , it would have been *prima facie* obvious to the skilled artisan at the time of the invention to modify the reagent system taught by Urdea et al. by substituting the antibody reagent taught by Fliss et al. for the capture probe of Urdea et al. The skilled artisan would have been motivated to make this modification in order to take advantage of the benefits of an antibody based nucleic acid detection system which benefits are recited by Fliss et al. in column 2 on p.2704.

Claim 26 is drawn to an embodiment of Claim 25 wherein the reagent system also comprises a reagent capable of converting double stranded nucleic acids present in the test sample into single stranded form.

Urdea et al. teach this limitation wherein they teach the use of 1M NaOH to denature the nucleic acids present in their reagent system. See Urdea et al. Column 26, beginning in Section F.

8. **Claim(s) 27-28** are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al. [US Patent No. 5,124,246 (JUN 1992)] in view of Fliss et al. (AUG 1993), as applied to Claims 25-26 above, and further in view of the Stratagene Catalog (1993).

Claim 27 is drawn to a diagnostic kit for detecting a polynucleotide in a test sample which is to comprise four components:

[1]a primary nucleic acid probe that is to comprise at least one single stranded base sequence that is substantially complementary to the target sequence to be detected.
[2]an antibody reagent capable of binding to hybrids formed between the primary probe and any particular polynucleotide target sequence present in the sample. Said antibody reagent must be incapable of binding substantially to single stranded nucleic acids.
[3]an amplification probe comprising at least two regions of nucleic acid sequence including at first sequence complementary to a sequence on said primary probe and a second region which is to include a plurality of discretely labalable sequence units.
[4]a labeling probe which is to comprise a detectable label and sequence complementary to sequences on the amplification probe.

Urdea et al. in view of Fliss et al. teach a reagent system which comprise all of components of the claimed diagnostic kit as argued above in ¶7. Urdea et al. in view of Fliss et al. do not teach assembling a kit from all of the components of said reagent system. However, the Stratagene catalog does teaches the advantages of assembling a kit with which to perform experiments in molecular biology. Therefore, absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to the place the appropriate reagents for performing the method taught by Urdea et al. in view of Fliss et al. into separate containers and then package the containers into a kit for the expected benefits of convenience and cost-effectiveness.

Claim 28 is drawn to an embodiment of Claim 27 wherein the diagnostic kit also comprises a reagent capable of converting double stranded nucleic acids present in a test sample into single stranded form.

Urdea et al. teach this limitation wherein they teach the use of 1M NaOH to denature the nucleic acids present in their reagent system. See Urdea et al. Column 26, beginning in Section F.

9. **Claim(s) 29** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al. [US Patent No. 5,124,246 (JUN 1992)] in view of Fliss et al. (AUG 1993) and the Stratagene Catalog (1993), as applied to Claims 27-28 above, and further in view of Pardos et al.[US Patent no. 5,084,565 (JAN 1992)].

Claim 29 is drawn to an embodiment of Claim 27 wherein the diagnostic kit is useful for the detection of *E. coli* in food wherein the kit further comprises a primary probe that comprises a nucleic acid sequence complementary to a sequence unique to *E. coli*.

Urdea et al. in view of Fliss et al. and the Stratagene Catalog, as applied to Claims 27-28 above, teach all of the limitations of Claim 29 except these references do not teach a primary probe that

comprises a nucleic acid sequence complementary to a sequence unique to *E. coli*. However, Urdea et al. do teach detecting the bacteria *N. gonorrhea* using a primary probe that comprises a nucleic acid sequence complementary to a sequence unique to *N. gonorrhea*. In addition, Pardos et al. teach probes for the specific detection for *E. coli*. Therefore, in the absence of an unexpected result , it would have been *prima facie* obvious to the skilled artisan at the time of the invention to modify the kit taught by Urdea et al. in view of Fliss et al. and the Stratagene Catalog by replacing the primary probe of Urdea et al. that comprises a nucleic acid sequence complementary to a sequence unique to *N. gonorrhea* for one that comprises a nucleic acid sequence complementary to a sequence unique to *E. coli*. The skilled artisan would have been motivated to make this modification in order to detect contaminating *E. coli* in food products.

DOUBLE PATENTING

10. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. **Claim(s) 25-29** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of the patent issued to Pandian et al. [U.S. Patent No. 6,306,657(2001)] . Although the conflicting claims are not identical, they are not patentably distinct from each other.

CONCLUSION

12. **Claim(s) 1-4 and 25-29** is/are rejected and/or objected to for the reason(s) set forth above.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Ethan Whisenant, Ph.D.
Primary Examiner
Art Unit 1634